

AP20Rec'd PCT/PTO 35 JUN 2006

to present their own antigens to professional antigen presenting cells, such as dendritic cells. Such antigen presentation can lead to the development of a response of the immune system toward these immunizing antigens. Many reports have demonstrated the usefulness of adjuvants to boost the immune response toward the killed cells. Among others, pertinent references such as works by Korbely (Korbely *et al*, *Laser Med. Surg*, 14 (1996), 329-334, *Can. Res.*, 56, (1996) 5647-5565; Chen *et al*, *SPIE*, 394 (2000), 26-32), as well as Nordquist *et al* (International Patent Applications published under Nos. WO 96/31237 and WO 99/47162A1) have demonstrated the usefulness of such an approach. Moreover, the usage of oxygenated species in blood components has been described previously using ozone as the chemical agent in conjunction with irradiation (Zee *et al*, US Patent No. 4,632,980; Fish *et al*, US Patent No. 4,831,268, Mueller *et al*, US Patent No. 4,968,483). Photodynamic Therapy has also been extensively described in "Photosensitizing Compounds: their Chemistry, Biology and Clinical uses" (1989, John Wiley & Sons, Chichester, UK, ISBN 0471923087). Many other pertaining references relating to the usage of Photosensitizers in the treatment of tumor masses combined with antibodies (Levy *et al*, US Patents Nos. 5,095,030 & 5,283,225) as well as ligands and antibodies (Pendry *et al*, US Patent No. 5,241,036). Autoimmune vaccines have been described by Bolton, A.E. (US Patent No. 6,204,058B1) (International Patent Application published under No. WO 98/07436) on which Rheumatoid Arthritis is treated using leukocytes with increased expression of specific antigens by oxidizing agents, UV irradiation and high temperature.

Extracorporeal Photopheresis has been described as a successful therapy for the treatment of Hepatitis C, in combination with other means such as Interferon alpha (O'Brien, C.B. International Patent Application published under No. WO 97/37654; McLaughlin S.N. *et al*, International Patent Application published under No. WO 97/36634), as well as in the treatment of other illnesses mediated by undesired activated immune cells (McLaughlin *et al*, US Patent No. 5,984,887 and Bisaccia *et al*, US Patent No. 5,426,116). Other studies have been reported regarding the usage of extracorporeal Photopheresis in indications such as organ

necrosis. Since mainly activated cells will be eradicated by photoactivatable molecules of the present invention (TH9402 and derivatives thereof), analysis of the cell population undergoing apoptosis and necrosis has been evaluated. Data indicates that B-cells, dendritic cells and activated T-cells among others, are rapidly eliminated. This advantage is exploited by inducing the immune system to produce an immune response against autoreactive T-cells. This property has been used in mice models and humans developing GvHD. Peripheral blood cells from individuals with GvHD are harvested, usually by leukopheresis, and exposed to PDT. These treated cells are then reinfused into the individual and this procedure is repeated at regular intervals. This treatment leads to improvement of GvHD that occurs after stem cell transplantation. PDT using photoactivatable molecules of the present invention (TH9402 and derivatives thereof) is able to prevent the development or treat GvHD in mice that received PDT-treated cells at regular intervals. This leads to improved survival of mice infused with PDT-treated cells. In contrast, mice receiving either non-PDT treated cells or media alone are developing GvHD leading to death. This is also shown in Figs. 1A and 1B using Kaplan-Meier survival analysis.

The present invention will be more readily understood by referring to the following examples which are given to illustrate the invention rather than to limit its scope.